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## The assessment of lung maturity in infants of diabetic mothers, by means of L/S ratio determination in tracheo-pharyngeal aspirate

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The respiratory distress syndrome (RDS) is more common in the newborns of diabetic mothers [3, 8, 9, 15]. Recent studies have shown that this increased incidence depends neither on the gestational age nor on the delivery route [5, 12, 13]. In view of these facts, the evaluation of lung maturation in the fetuses of diabetic mothers seems to be of the utmost importance. However, it is rather difficult to assess correctly the maturity of fetal lungs by the accepted methods, since, not infrequently, lung maturation is delayed in these fetuses, and L/S values, which usually indicate fetal lung maturation, may fall to below critical levels [11, 16].

We therefore suggest that, in addition to the commonly employed method of evaluation of fetal lung maturity, i.e., amniotic fluid analysis, examination of the tracheo-pharyngeal aspirate should also be performed in the newborn of every diabetic mother, at the time of delivery.

### 1 Material and Method

This group comprised 15 pregnancies complicated by diabetes mellitus of all degrees of severity (A, B, C, D) according to the classification of WHITE. Ages of the patients ranged between 36 and 40 weeks.

In all patients the L/S ratio was determined in the amniotic fluid once or several times prior to

### Curriculum vitae

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delivery, as well as in the tracheo-pharyngeal aspirate immediately after birth of the baby.

In all cases the foam test was done in the amniotic fluid and, in those cases in which there was a sufficient volume of tracheopharyngeal aspirate, the foam test was performed in the latter as well.

The L/S determination was carried out as follows: After extraction in a mixture of chloroform and ethanol and precipitation in acetone, phospholipids were separated on silicagel G plates. The separated sphingomyelin and lecithin were collected from the plates, their ratio being determined by the phosphate ratio determination. The method is based on the reaction between phosphoammoniummolybdate and  $\alpha$ -aminonaphtolsulphonic acid reagent.

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The foam test was done by the CLEMENTS method [1].

## 2 Results

Tab. I details the results of the different determinations in the amniotic fluid as well as in the tracheopharyngeal aspirate, according to the degree of severity of the diabetes mellitus, gestational age and the route of delivery; furthermore, the clinical condition of the neonate as far as the respiratory state was concerned was evaluated and noted following the delivery.

It is obvious from this table that according to the foam test and L/S ratio in the amniotic fluid, all fetuses supposedly had normally matured lungs. However, when these two tests were done in the tracheopharyngeal aspirate, the results indicated lack of full lung maturity in 4 cases.

In fact, all these 4 newborns developed the RDS (Cases 3,6,10,14). The syndrome occurred in babies born between the 36th to 38th weeks of gestation, in cases of diabetes of severity levels A,B,C of the White classification.

## 3 Comment

In spite of the increased exposure to the respiratory distress syndrome of neonates born to diabetic mothers, there is to date no reliable test which might be capable of determining the baby's true respiratory condition in such pregnancies.

The L/S ratio and foam test in the amniotic fluid unfortunately lack reliability, in view of the possibility of values, which had shown pulmonary maturity, falling to below the critical value proving such maturity. Other methods which might possibly prove to be more accurate in diabetic pregnancy, such as that indicating phosphatidyl glycerol concentration in the amniotic fluid or in pulmonary secretions [6,7] are not as yet in wide use.

The cause of delay in lung maturation or decrease in the degree of maturation in the fetus of diabetic gestation is not quite clear. The accepted opinion is that which involves insulin, in view of an inhibiting effect of this hormone on the lecithin synthesis stimulatory effect of cortisol. Moreover, it is possible that factors other than fetal hyperinsulinism interfere with the synthesis of pulmonary surfactant.

Tab. I. The incidence of R.D.S. and lung maturity in 15 cases of diabetes in pregnancy.

No.	Gestational Age (weeks)	Class of Diabetes	Route of Delivery	Amniotic Fluid		Pharyngo-tracheal aspirate		Respiratory Distress Syndrome
				L/S	foam test	L/S	foam test	
1	39	A	vaginal	2.7	(+)	3.1	(+)	No R.D.S.
2	38	A	vaginal	2.2	(+)	3.4	(+)	No R.D.S.
3	38	A	vaginal	2.9	(+)	1.7	(-)	Mild R.D.S.
4	39	A	vaginal	2.0	(+)	2.4	(+)	No R.D.S.
5	37	B	C.S.	3.1	(+)	3.7	not done	No R.D.S.
6	36	B	C.S.	2.3	(+)	1.5	(-)	Severe R.D.S.
7	37	C	vaginal	3.2	(+)	4.1	(+)	No R.D.S.
8	36	C	C.S.	3.2	(+)	3.3	not done	No R.D.S.
9	36	C	C.S.	2.2	(+)	2.1	(±)	No R.D.S.
10	36	C	C.S.	2.2	(+)	1.2	not done	Severe R.D.S.
11	36	D	C.S.	2.7	(+)	3.7	(+)	No R.D.S.
12	37	D	C.S.	2.0	(+)	2.6	not done	No R.D.S.
13	37	D	C.S.	3.4	(+)	3.6	(+)	No R.D.S.
14	37	D	C.S.	2.5	(+)	1.7	(±)	Mild R.D.S.
15	37	D	C.S.	2.8	(+)	3.3	(+)	No R.D.S.

MUELLER-HEUBACH et al. [10] and DAHLENBURG et al. [2] find the L/S ratio determination for assessment of fetal lung maturation unreliable in pregnancies complicated by diabetes. GABBE et al. [3] and TCHOBRUTSKY et al. [14], on the other hand, claim that L/S ratio determination in amniotic fluid of diabetic women is a useful advance in the management of diabetic pregnancies.

Results of this study indicate that the assessment of lung maturity in diabetic pregnancy, by means of the tracheo-pharyngeal aspirate (as a complement-test to those done prior to birth), may possibly contribute markedly to the follow-up and management of these high-risk babies in the immediate neonatal period. Moreover, such a complement-test permits the obstetrician and neonatologist a fair, more accurate prognostic evaluation, as to the risks that the newborn runs of developing RDS. Thus, in hospitals which do not have a special intensive-care unit for the newborn, this test may give advance warning as to which

baby should be referred at the earliest opportunity to a Medical Center equipped with the means to manage neonatal respiratory complications.

Since this test is simple and non-invasive, it is to be recommended in babies of all degrees of severity of diabetes, and in all gestational ages. In spite of our relatively small group of patients in this study, the test appears to be reliable, since there were no false-positive or false-negative results. It should be noted that the limitations of this method are mainly the rather small volume of aspirate from the pharynx and trachea, as well as the possibility of blood or meconium staining of the fluid.

We believe that in view of the simplicity and reliability of the evaluation of fetal lung maturity by means of tracheo-pharyngeal aspirate in diabetic pregnancy, and because of the lack of other reliable means of assessment of lung maturity, this test has a place in the management of diabetic pregnancy and delivery.

### Summary

The respiratory distress syndrome is more common in the newborns of diabetic mothers. The comparatively high rate of incidence of this syndrome depends neither on gestational age nor delivery route. In view of these facts, the evaluation of fetal lung maturation of diabetic mothers seems to be of the utmost importance.

The methods usually employed for the determination of fetal lung maturation are of limited value, because occasionally L/S ratio values, which usually indicate fetal lung maturation, may fall to below critical levels. It is, therefore, extremely important to assess lung maturity in the newborn of a diabetic mother at the time of delivery.

In 15 pregnancies complicated by diabetes mellitus of all degrees of severity (A–D), according to the classification of P. WHITE, L/S ratio in amniotic fluid prior to delivery

was determined. L/S ratio was determined in tracheo-pharyngeal aspirate, as well, soon after delivery. In all cases the foam stability test was done in the amniotic fluid before delivery and, when there was a sufficient quantity, also in the tracheo-pharyngeal aspirate.

According to the foam test and L/S ratio in the amniotic fluid, all fetuses supposedly had normally matured lungs. Nevertheless, according to these two tests in the tracheo-pharyngeal aspirate, results indicate lack of full lung maturity in four cases. In fact, all these four newborns developed the respiratory distress syndrome.

This test appears to be reliable, simple and non-invasive, and is therefore recommended in babies with diabetes of all degrees of severity, and in all gestational ages.

**Keywords:** Foam test, L/S ratio, lung maturation, respiratory distress syndrome.

### Zusammenfassung

**Lungenreifediagnostik bei Kindern von Diabetikerinnen durch L/S-Ratio-Bestimmungen im tracheo-pharyngealen Aspirat**

Das Atemnotsyndrom (synonym: RDS) tritt gehäuft bei Neugeborenen von diabetischen Müttern auf. Die vergleichsweise hohe Rate hängt weder vom Gestationsalter noch vom Geburtsverlauf ab. Unter Berücksichtigung dieser Tatsachen scheint die Bestimmung der fetalen Lungenreife bei Diabetikerkindern von äußerster Wichtigkeit.

Die gebräuchlichen Methoden in der Lungenreifediagnostik haben lediglich eine begrenzte Aussagekraft, denn L/S-Werte, die normalerweise die vorhandene Lungenreife anzeigen, können gelegentlich in kritische Bereiche absinken. Es ist deshalb ausgesprochen wichtig, den Lungenreife-status von Diabetikerkindern kurz nach der Entbindung einschätzen zu können.

In 15 Schwangerschaften, deren Verlauf durch einen Diabetes mellitus mit unterschiedlichen Schweregraden

(A–D; Zuordnung nach WHITE) kompliziert war, wurden kurz vor der Geburt L/S-Ratio-Bestimmungen im Fruchtwasser durchgeführt. Gleich nach der Geburt wurden die L/S-Werte im tracheo-pharyngealen Aspirat bestimmt. Auf alle Fruchtwasserproben wurde außerdem der Schaumtest angewandt. Bei ausreichenden Mengen von tracheo-pharyngealem Aspirat konnte der Schaumtest ebenfalls kurz nach der Geburt durchgeführt werden.

Nach den Ergebnissen des Schaumtests sowie der L/S-Ratio-Bestimmung in den Fruchtwasserproben konnten

wir bei allen Kindern einen normalen Lungenreifstatus erwarten. Die Bestimmung, im tracheo-pharyngealen Aspirat ergab jedoch in 4 Fällen Schaumtest- bzw. L/S-Ratio-Werte, die eine mangelnde Lungenreife anzeigten. In der Tat entwickelte sich bei diesen 4 Kindern ein RDS. Der verwendete Test erscheint zuverlässig, leicht zu handhaben und ist dabei nicht invasiv. Er empfiehlt sich daher zur Lungenreifediagnostik bei Kindern von Diabeticerinnen, unabhängig vom Schweregrad des Diabetes und vom Gestationsalter.

**Schlüsselwörter:** Atemnotsyndrom, L/S-Ratio-Bestimmung, Lungenreife, Schaumtest.

## Résumé

**Evaluation de la maturité pulmonaire chez les bébés de mères diabétiques par la détermination du rapport L/S dans le liquide trachéo-pharyngien aspiré**

L'asphyxie périnatale est plus fréquente chez les nouveau-nés de mères diabétiques. Le taux relativement élevé d'incidence de ce syndrome ne dépend ni de l'âge de gestation, ni du déroulement de l'accouchement. En considération de ces faits, il semble bien que l'évaluation de la maturation pulmonaire foetale chez les mères diabétiques soit de la plus grande importance.

Les méthodes employées habituellement pour la détermination de la maturation pulmonaire foetale sont d'une valeur limitée parce qu'il peut arriver que les valeurs du rapport L/S, qui servent en général d'indice pour la maturation pulmonaire foetale, tombent au-dessous du seuil critique. C'est pourquoi il est extrêmement important d'évaluer la maturité pulmonaire du nouveau-né d'une mère diabétique au moment de l'accouchement.

Dans quinze grossesses compliquées par un diabète mellitus à tous les degrés de gravité (A–D), [1 nous avons

déterminé [– selon le classement de P. WHITE –] le rapport L/S du liquide amniotique avant l'accouchement, ainsi que dans le liquide trachéo-pharyngien aspiré pu e après l'accouchement. Dans tous les cas, le test de stabilité d'écume a été effectué dans le liquide amniotique avant l'accouchement et dans le liquide trachéo-pharyngien aspiré – si on en disposait d'une quantité suffisante.

Si on en croit les résultats du test d'écume («foam test») et le rapport L/S du liquide amniotique, tous les foetus avaient une maturité pulmonaire normale, mais si on considère les données de ces deux tests appliqués cette fois dans le liquide trachéo-pharyngien aspiré, on constate que quatre de ces foetus n'avaient pas atteint la pleine maturité pulmonaire. Comme de fait, ces quatre nouveaux-nés ont manifesté une asphyxie périnatale.

La détermination du rapport L/S dans le liquide trachéo-pharyngien aspiré semble être un test sûr, simple et non-invasif, ce qui le fait recommander pour les bébés avec diabète de quelque degré de gravité que ce soit, et pour tous les âges de gestation.

**Mots-clés:** Asphyxie périnatale, rapport L/S, test d'écume.

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